REMARKS

Status of Prosecution

Claims 13, 24, and 29-71 are pending in the application and are rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite, and under 35 U.S.C. §103(a) as an allegedly obvious variant of Hollingsworth *et al.* (1995) Genes Dev. 9:1728-39 ("Hollingsworth"). Claims 24, 44, and 56 are canceled herein, without prejudice. Claims 13, 30-32, 34-37, and 68-71 are amended herein without the addition of new matter.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 13, 24, and 29-71 are rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Specifically, the Office Action states that claim 13 and 24 fail to set forth how the contacting occurs as there is allegedly no indication of in what system the MSH5 is contained, and it is allegedly unclear as what activity is being claimed. Applicants traverse the rejection. Nevertheless, in an effort to facilitate prosecution, Applicants have amended claims 13, 31, 34, 36, 68, and 70 to even more clearly indicate the system in which MSH5 is contained. Support for these amendments can be found throughout the specification, for example, at page14, lines 30-35. Applicants have amended claims 13, 30-32, 34-37, and 68-71 to even more clearly indicate what activity is being claimed. Support for the amendments can be found throughout the specification, for example, at page 18, lines 16-17.

Rejection Under 35 U.S.C. §103(a)

Claims 13, 24, and 29-71 are rejected under 35 U.S.C. §103(a) as allegedly an obvious variant of Hollingsworth. Specifically, the Office Action states that Hollingsworth teaches that MSH5 is a meiosis-specific gene, active to facilitate meiosis and meiotic chromosome synapsis in bacteria, yeast, and humans, that mutant MSH5 results in decreased spore/gamete viability, and that there is a direct relationship of MSH5 to meiosis and chromosome synapse in yeast, bacteria, and humans. In addition, the Office Action alleges that Hollingsworth suggests that inhibited or reduced activity of MSH5 inhibits meiosis, chromosome synapsis and decreased fertility. According to the Office Action, given these

alleged teachings of Hollingsworth, it would have been obvious to assay for a candidate for meiotic inhibition, and by extension, contraception by testing putative agents for their ability to inhibit MSH5. Applicants traverse the rejection.

Applicants respectfully assert that Hollingsworth does not teach that MSH5 is a meiosis specific gene that facilitates meiosis and meiotic chromosome synapsis in bacteria, yeast, and humans, and does not teach any relationship between MSH5 and meiosis in any organism other than yeast. Hollingsworth teaches only the identification of a yeast MutS homolog designated MSH5 that, according to their results, appears to facilitate reciprocal crossover between homologs. Hollingsworth does not teach or suggest the existence or function of MSH5 in organisms other than yeast, and does not teach or suggest a role for MSH5 in chromosome synapsis. Hollingsworth states only that previously-characterized MutS homologs function in mismatch repair in different organisms, including bacteria, yeast, and humans, and demonstrates that MSH5 does not function in mismatch repair (page 1729, first column). Thus, there is no connection of MSH5 to meiosis in bacteria or humans. Applicants previously detailed arguments on this point in their Request for Reconsideration dated September 3, 2000. Applicants note that the Examiner has not disputed their characterization of Hollingsworth and has not provided any argument or evidence as to why the Applicants' characterization is incorrect. Rather, the Examiner has simply repeated his earlier characterization of Hollingsworth, which Applicants respectfully maintain is incorrect.

Applicants respectfully disagree that there is any express or implied suggestion in Hollingsworth that inhibited or reduced activity of MSH5 inhibits meiosis and chromosome synapsis, and decreases fertility. Hollingsworth indicates that MSH5 mutants exhibit increased nondisjunction, decreased reciprocal crossover exchange, and decreased spore viability. There is no teaching or suggestion that mutations in MSH5 prevent or slow the rate of meiotic division or the pairing of homologous chromosomes. Indeed, the observed increase in nondisjunction is evidence that synapsis is not inhibited. In addition, spore formation in yeast is a form of asexual reproduction. As such, any apparent decrease in spore viability stemming from a mutation in MSH5 may have implications for reproduction of the yeast cell on the whole, but cannot be a suggestion for a decrease in fertility, a characteristic of sexual reproduction only.

Applicants respectfully assert that a *prima facie* case for obviousness has not been established. To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference; there must be a reasonable expectation of success; and the prior art reference must teach or suggest all of the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed Cir. 1991).

At least two of the three requisite elements of a *prima facie* case have not been established. First, Hollingsworth does not teach or suggest all of the limitations of the claimed invention. The invention relates to methods to identify compounds useful as a contraceptive, to inhibit meiosis in a cell, to prevent fertilization in a subject, to stimulate chromosome synapsis in a cell, and to inhibit chromosome synapsis in a cell. Hollingsworth does not teach or suggest any such methods. According to the Office Action, it would be obvious to assay for candidates for meiotic inhibition and for contraception by testing putative agents for their ability to inhibit MSH5 solely based on the teachings of Hollingsworth. As detailed above, Hollingsworth teaches only that MSH5 facilitates meiotic reciprocal crossover in a yeast cell. There is no teaching or suggestion that modulation of MSH5 would have any inhibitory effects on meiosis, would have any effect on fertility, would have any effect on chromosome synapsis, or would have any utility as a contraceptive in sexually reproducing organisms, and there is no teaching or suggestion to assay for such effects. Accordingly, all of the limitations of the claimed invention are not taught or suggested by Hollingsworth. Thus, a *prima facie* case for obviousness has not been established, and withdrawal of the rejection is warranted.

Second, there is no suggestion or motivation, either from the reference itself or from knowledge generally available in the art, to modify the teachings of Hollingsworth to arrive at the claimed invention. The mere fact that a reference can be modified does not render the modification obvious. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990). The reference does not expressly or impliedly suggest the desirability or feasibility of the claimed methods. Moreover, given that Hollingsworth does not teach or suggest that modulation of MSH5 would have any inhibitory effects on meiosis, would have any effect on fertility, would have any effect on chromosome synapsis, or would have any utility as a contraceptive in sexually reproducing organisms, those of skill in the art would not reason the inventive methods from

its teachings. Accordingly, there is no suggestion or motivation to modify the teachings of Hollingsworth to arrive at the claimed invention. Thus, a *prima facie* case for obviousness has not been established, and withdrawal of the rejection is warranted.

Conclusion

In view of the amendments submitted herewith and the foregoing remarks, Applicants respectfully assert that all claims presently pending are in condition for allowance. Favorable reconsideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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